



## THE USE OF CALMETTE'S ANTIVENENE IN SNAKE-BITE IN INDIA.

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On the 21st of January 1902 Captain Lamb, I.M.S., read a paper before our Society on "Snake Venoms: Their Physiological Action and Antidote" which you will find published at p. 220 of Vol. XIV of this Journal. In this paper he showed that the antivenene prepared by Calmette, of the Pasteur Institute at Lille, was useful when administered in time and in sufficient amount, in cases of cobra bite, but useless as an antidote for Daboia poison. In Vol. XV of the Journal at p. 112 appears an article by Fleet-Surgeon P. W. Bassett-Smith, R.N., entitled "Snake-bites and Poisonous Fishes" in which it is stated, on the authority of Calmette, that his antivenene was capable of protecting "animals and man from lethal doses of *any* venom, although each snake venom has, *per se*, well marked toxic peculiarities producing several and various local phenomena."

Naturally these contradictory statements appearing in the Journal of the Society have caused perplexity to some of the members, and the Secretary has asked me, in the absence of Captain Lamb, to give a short account of his investigations, and to reconcile the two statements if possible.

It must be said here that Bassett-Smith's article was originally published in 1902 in the *Encyclopædia Medica* and, therefore, can only represent the state of our knowledge prior to that date, and that he could not possibly know of Captain Lamb's results, as these were not published till a later period.

Having cleared the way by these preliminary remarks let me present to you, by means of these tables, a bird's-eye view of the various ways in which venoms of some of the Indian snakes act.

I can only give tables of the actions of the venoms of cobra (*Naja tripudians*), Russell's viper (*Daboia Russellii*) and banded krait (*Bungarus fasciatus*) as these are all that Captain Lamb has yet been able to deal with, owing to the difficulty of collecting material. This is, I think, a matter, so full of importance to the well being of India, that the Society would do well to represent it in the proper quarter, and so help Captain Lamb to complete his series of valuable investigations, by

calling the attention of Government to the necessity of assistance in collecting live venomous snakes, for the purpose of extracting their poison.

**Cobra Venom—**

1. Acts on central nervous system, i.e., the brain and spinal cord. This causes paralysis of the limbs, then of the muscles of respiration. The heart continues to beat long after the breathing has stopped.
2. Acts on the blood also, causing a breaking up of the red corpuscles of the blood, and a lengthening of the time the blood takes to coagulate. These physiological effects are of little importance as far as the symptoms of cobra venom intoxication are concerned.
3. Causes death in from 3 to 6 hours after the bite is inflicted as a rule, though this period may be as long as a day or two.
4. Does not produce symptoms immediately,—an interval, generally of an hour or two, elapsing before they appear, during which treatment may be applied.
5. Breaks up general tissue cells, such as those of the kidneys, liver, etc. This is a property common to all the venoms worked with up to date.

**Daboia Venom—**

1. Does not produce definite symptoms pointing to direct action on the nervous system. Whether there is any action at all, is now being worked out.
2. Acts on the blood plasma, the corpuscles, the walls of the small blood vessels (capillaries) and the heart. In acute cases the symptoms produced are, giddiness followed at once by violent convulsions and gasping for breath, death resulting in a few seconds.
3. The cause of death in these cases\* is from clotting of the blood in the pulmonary arteries and some of the other blood vessels.
4. When the dose is not large enough to cause this intravascular clotting, death (a) may ensue in a few hours from failure of the heart or (b) may follow after a longer time, from the distinctive action of the poison on the red corpuscles, and capillary walls allowing the blood to exude, and producing oedema and hæmorrhage, in many parts of the body, and its further action in preventing the proper coagulation of the blood. Death is also frequently due to bacterial invasion causing septicæmia, malignant oedema, etc. This invasion of bacteria is due to the fact that locally, at the site of inoculation, the tissues die and a large slough forms.  
The corpuscles are largely destroyed and the fluid part of the blood stained red by their colouring matter.
5. Other cells of the body are also broken up, as with other snake venoms.

**Banded Krait Venom—**

1. Acts on the central nervous system much in the same way that cobra venom does. Profuse salivation and vomiting is common. Paralysis with twitching of muscles comes on, and death ensues from paralysis of respiration in two or three days.
2. Acts on the blood in almost the same way as Daboia venom does (if injected in very large doses), causing death in a few minutes from extensive clotting of the blood in the pulmonary arteries and right side of the heart. The red cells of the blood, however, are only acted on in a quite minor degree, and no symptoms observable during life are produced by this.
3. Or serious symptoms may not come on for some days, but there is loss of appetite and weight, followed by great depression, marked diminution in the urinary secretion, slight failure of respiratory functions, irregular elevations of temperature, great muscular weakness and paralysis.  
Purulent discharges from eyes, nose and rectum are also seen.  
Death ensues in from 6 to 12 days. In these cases it has been found that there occurs "a well marked primary degeneration of the cells of the central nervous system." (1)

\* Note.—This action will probably only be seen in experiments on animals; under natural conditions the amount of venom injected will be insufficient to produce such extensive clotting. It results when a sufficient amount of venom is injected into the blood stream directly.

From a study of these tables one realises how differently snake venoms act—one acting through the nervous system with incredible rapidity, another requiring some days to produce its equally fatal results, while a third acts almost entirely on the blood.

Realising this then, is it much wonder that scientists looked askance on Calmette's sweeping assertion, that his antivenene was useful for the bites of all poisonous snakes; knowing, as they did, that the venom used by him to produce immunity in the horse was that of the cobra, with only small additions of other snake venoms? (2)

Behring, the great authority on serum-therapy, and whose name you must all be familiar with in connection with anti-diphtheritic serum, lays it down as a law that "the action of an immunising serum is specific"; that is, in other words, an immunising serum is only useful in the case of the disease or toxine by means of which it has been prepared, *e.g.*, anti-diphtheritic serum is only of use against diphtheria, not against plague or tetanus or any other bacterial disease.

Everyone now admits this, so it is not astonishing to find that a serum prepared by injecting a horse with the nerve-destroying cobra venom should be quite inactive in cases of poisoning by the blood-destroying Daboia poison.

The first published account of experiments undertaken to investigate this point was by Professor C. J. Martin, of Melbourne, now Director of the Lister Institute, London (Inter-Colonial Med. Journal of Australasia, Augt. 20, 1897, and Apl. 20, 1898), who showed that Calmette's serum was useless against the poison of the Australian tiger snake (*Hoplocephalus curtus*).

Since then, Tidswell, of Sydney, has proved (3) that it is equally useless for the other poisonous snakes of Australia. He has gone a step further, however, for he manufactured a serum by injecting a horse with *Hoplocephalus* poison, which was highly effective in preserving animals from the effects of that poison, but wholly useless against three other Australian snakes, *viz.*, the brown snake, the black snake (*Pseudechis*) and the death adder (*Acanthophis*), though these belong to the same sub-family Elapinae of the Colubrine class.

These observations have been further extended by Captain Lamb, I.M.S., who, working with serum sent to him by Dr. Tidswell, proved that this *Hoplocephalus* serum (4) "has no neutralising power for the

venoms of three of our Indian snakes, *viz.*, *Naja tripudians* (cobra), *Bungarus fasciatus* (banded krait), and *Daboia Russellii* (chain viper).” Now this serum had been made by the use of one kind of venom only and was, therefore, better fitted for testing the question of specificity than Calmette’s, which is prepared by using cobra venom mixed in varying proportion with that of other serpents. The amount of cobra venom, used, however, appears to be so preponderating, that for practical purposes it also may be regarded as a specific serum, useful only against this one kind of poison.

In the paper communicated by Captain Lamb to our Journal, you will find an account of how the serum is procured and the method of using it in cases of cobra bite. I need not, therefore, go over that ground again, but would merely remind you, that if given in sufficiently large doses, and before symptoms of the venom intoxication have become pronounced, we have in Calmette’s antivenene a safe and good remedy for cobra bite.

But alas! when we turn to the other dangerous snakes of India we find the serum wholly useless. Captain Lamb and Dr. Hanna, (5) working together in the Parel Laboratory, have conclusively proved that antivenene is powerless to prevent death in animals poisoned by the venom of the chain viper (*Daboia Russellii*). Since then Captain Lamb (4) has been able to test Calmette’s antivenene against the poisons of the banded krait (*Bungarus fasciatus*) and the phoorsa (*Echis carinata*).

I need not describe the long series of experiments by which he proved his point; those of you who desire to read of these must go to the original paper, published by Government as No. 5 of the New Series of Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India. Those of us who know the experimenter and his careful methods will realise the weight that must be given to his conclusion, that Calmette’s antivenene (p. 5) “is of no value whatever in the treatment of cases of bites from *Daboia Russellii*, *Bungarus fasciatus*, or *Echis carinata*.”

In summing up his observations on Calmette’s antivenene and Tidswell’s *Hoplocephalus* serum he says: (p. 6) “We have seen that the Australian snakes belong to the same sub-family, but to different genera as the cobra and the banded krait. Those results therefore, taken along with the results collated above, got with Calmette’s serum, show conclusively that the serum prepared with the venom of any one genus of

poisonous snake is specific for the venom of that genus and is inactive for the poisons of other genera. It still remains to be shown if a serum prepared with a single venom would be specific for the venom of that species, that is to say, inactive for the poisons of other species of the same genus."

Since this was written, Captain Lamb tells me he has been able to test antivenene prepared with pure cobra venom, against the venom of the king cobra (*Naia bungarus*), and that to a very large extent it appears to be inactive, though, as we have seen, useful for bites by the cobra (*Naia tripudians*), a different species of the same genus.

This, if confirmed by further research, will go to prove that the antivenomous serums produced up to the present are absolutely specific, and only useful for the particular poison which called them into existence.

You will realise, then, that the question of a cure for bites by Indian snakes is not a simple one, but that it will require perhaps years of patient research for its elucidation, and not till such work is accomplished can we hope to have placed in our hospitals a cure for the victims of these dreaded accidents.

#### REFERENCES.

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3. A Preliminary Note on the Serum-Therapy of Snake-bite by Frank Tidswell, M.B., Ch.M., D.P.H., Principal Assistant Medical Officer of the Government, and Microbiologist to the Board of Health, N.S.W., Sydney. Australasian Medical Gazette, April 21st, 1902.
4. Specificity of Antivenomous Sera. By George Lamb, M.D., (Glasg.), Captain, I.M.S. No. 5, Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India. Calcutta, Office of the Superintendent of Government Printing, India, 1903.
5. Journal of Pathology and Bacteriology; Edinburgh and London, 1902, Volume VIII, page 1.